REMARKS

Claims 1-22 are pending in this application and have been examined. Claims 1-22 stand rejected. Reconsideration and allowance of Claims 1-22 in view of the following remarks is respectfully requested.

The Rejection of Claims Under 35 U.S.C. § 103(a)

1. Claims 1, 2, 4, 7-9. 11, 13-15, 17, 20, and 21

The Examiner has rejected Claims 1, 2, 4, 7-9, 11, 13-15, 17, 20, and 21 under 35 U.S.C. § 103(a) as obvious over U.S. Patent No. 5,849,484 (Leibowitz et al.) in view of U.S. Patent No. 5,525,468 (McSwiggen et al.). According to the Examiner, Leibowitz et al. describes a method of inhibiting the self-splicing of Group I introns using an inhibitor compound. The Examiner acknowledges that Leibowitz et al. does not describe an inhibitor compound that is an oligonucleotide. However, the Examiner has indicated that such an oligonucleotide is described in McSwiggen et al. and that it would have been obvious to substitute the oligonucleotide of McSwiggen et al. in the method of Leibowitz et al.

Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness. There are three requirements for establishing a *prima facie* case of obviousness. First, there must be some suggestion or motivation, either in the references themselves or in knowledge generally available to one of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success. Third, the prior art reference must teach or suggest all the claim limitations.

Applicants' invention provides methods and compositions for inhibiting the self-splicing reaction of Group I introns using oligonucleotides that mimic the 5' exon guide sequence of these introns. Specification, page 3, lines 12-14. Independent Claim 1, from which Claims 2-7 depend, is directed to an inhibitor of a Group I intron splicing reaction comprising an

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oligonucleotide that is capable of binding with the 5' internal guide sequence of the precursor RNA and of being trans-spliced to the 3' exon of the precursor RNA. Independent Claims 8 and 14, from which Claims 9-13, and 15-19 depend, respectively, are directed to methods for inhibiting self-splicing of a Group I intron using an oligonucleotide that trans-splices to the 3' exon of the precursor RNA. Independent Claim 20, from which Claims 21 and 22 depend, is directed to designing an inhibitor of Group I intron splicing comprising choosing and preparing an oligonucleotide that is capable of binding with the 5' internal guide sequence of the precursor RNA and of being trans-spliced to the 3' exon of the precursor RNA.

Applicants respectfully submit that the cited references, alone or in combination, fail to teach or suggest applicants' claimed invention. As noted by the Examiner, Leibowitz et al. does not describe any inhibitor compound that is an oligonucleotide. Thus, in contrast to the assertion made in the paragraph bridging pages 2 and 3 of the Office action, Leibowitz does *not* disclose a compound "capable of binding with the 5' internal guide sequence of the precursor RNA and of being trans-spliced to the 3'-exon of the precursor RNA." Inspection of the various sections of Leibowitz cited as supporting this assertion reveals that none of these actually describes such compounds. Although acknowledging that Leibowitz et al. does not teach oligonucleotides, the Examiner characterizes McSwiggen et al. as disclosing an oligonucleotide that is capable of binding with the 5' internal guide sequence of the precursor RNA and of being trans-spliced to the 3' exon of the precursor RNA. Applicants respectfully disagree and suggest that a closer reading of McSwiggen et al. reveals that its teaching is actually unrelated to the presently claimed compositions and methods.

Specifically, McSwiggen et al. is directed to methods for designing a class of enzymatic cleaving agents (ribozymes) that exhibit a high degree of specificity for an RNA target site. An RNA target site is defined as a sequence in a target RNA that is targeted for cleavage.

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McSwiggen et al., Column 7, lines 34-40. McSwiggen et al., Column 6, lines 20-25. To circumvent the expensive process of manufacturing ribozymes that are specific for an RNA target site that may later be found not be accessible to the ribozyme, McSwiggen et al. describes methods for determining the accessibility of a desired RNA target site to a ribozyme using oligonucleotides as a proxy for the ribozyme. McSwiggen et al., Abstract; Column 6, lines 48-60. RNA target site accessibility is assessed by contacting the RNA target site with a DNA oligonucleotide complementary with the RNA target site in the presence of a cleaving agent that will specifically cleave RNA/DNA duplexes. Cleavage of an RNA target site indicates that the RNA target site is potentially accessible to a ribozyme containing sequences within its substrate-binding domain that are complementary to the RNA target site. McSwiggen et al., Column 7, lines 19-32. Accordingly, McSwiggen et al. uses an oligonucleotide as an assay to determine whether a specific RNA target site is susceptible to cleavage by a ribozymes that includes the oligonucleotide sequence in its substrate-binding domain. Therefore, the oligonucleotides used by McSwiggen et al. bind to whatever RNA has been selected as a potential target for development of a ribozyme effector molecule.

McSwiggen et al. neither teaches nor suggests an oligonucleotide that is capable of binding with the 5' internal guide sequence of a Group I intron in a precursor RNA to inhibit self-splicing of the Group I intron, as required by Claims 1, 2, 4, 7, 20, and 21. McSwiggen et al. does not even mention Group I introns as potential targets for the hammerhead ribozymes that it discusses. Nor does McSwiggen teach or suggest an oligonucleotide that is capable of being trans-spliced to the 3' exon of such a precursor RNA, as required by Claims 1, 2, 4, 7-9, 11, 13-15, 17, 10, and 21. Therefore, the cited references, alone or in combination, fail to teach or suggest all the limitations of applicants' claimed invention. For this reasons, applicants respectfully request withdrawal of this ground of rejection.

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